12th Annual IMWG 2021 – Held Virtually

* The International Myeloma Working Group, which consists of nearly 150 members (MM expert doctors from around the world) met virtually June 22-23, 2021 to develop research initiatives and guidelines for doctors treating MM patients. IMWG Chairmen: Drs. B Durie, SV Rajkumar, P Moreau, and J San Miguel. Members from the SF Bay Area include Drs. T Martin (UCSF), N Shah (UCSF), and S Sidana (Stfd). I was able to attend all but the last couple of hours of the meeting, so will report my takeaways from the Plenary Sessions and Working Committees (which also met a month earlier to consider possible initiatives). Missing Sessions: Novel MM Treatments and Strategies for Disease Management.

Plenary Sessions

SMM

- The IMF has developed an on-line app for physicians called My Risk that calculates a patient's risk of progression to MM.
- Revlimid or Revlimid-dex (and not observation) should be considered the Standard of Care for High Risk SMM.
- What should the clinical trial endpoint be for HR SMM…sustained MRD-, end organ damage?

Frontline

- Early or delayed (at first relapse) SCT doesn't appear to make a difference in Overall Survival (OS) but Dr. Rajkumar still favors early SCT because:
  - Progression Free Survival is better
  - Lower age and better performance status
  - Benefit for HR MM?
  - Patient preference
  - Best of both worlds, allowing 1 SCT now and 1 later.

  "But we cannot tell patients that early SCT will result in longer OS." -SVR

MRD

- Sustained MRD is the most important factor to making treatment decisions. (Sustained for 1 yr, 2 yrs, longer?)
- If one arm of a clinical trials has twice the MRD- results, does that mean that it would also have twice the PFS? That's the goal if MRD is to be used as a surrogate for PFS.

CAR-T Therapy

- While we can't compare Ide-cel and Cilta-cel across trials, a median PFS difference of 9 mos versus 22 mos is quite significant.
- "Why is there a disconnect between MRD- with CAR-T vs MRD- in every other treatment? Because CAR-T only reaches the bone marrow (where MRD is measured) and not other areas." N Munshi
- "Day 28 MRD testing should be changed to Day 100. Even MRD at 6 mos or 12 mos might be more useful." S Lonial

New Monoclonal Antibodies

- Photophobia = light sensitivity vs Keratopathy = blister swelling on the cornea
- These bispecific antibodies really have high single agent responses (typically double the rates when Velcade, Revlidmid, and Dartumumab were approved).

Working Committees

SMM

- "The only Phase 3 results we have for HR SMM are the Rev or Rev-dex results. We can't start using other MM treatments until we have other Phase 3 readouts." SVR
- CESAR and ASCENT trials will have some MRD readouts at ASH21.
- From Working Committee Meeting:
  - After 5 years, reduce visits from every 3 mos to every 6 mos.
  - Circulating plasma cells increases the risk to progression…we need a trial to establish the cutoff.
  - Bisphosphenates every 3 mos for 2 yrs for HR SMM?
  - Re trial design, are SMM pts who progress considered "relapsed" for participation in MM trials? Not presently.

Bone Disease

- We need a better response definition of plasmacytomas.
- PET-CT vs DWI-MRI…prefer for patients to get both.
- Focal lesions (inside the bone marrow, detected by MRI) lead to the development of lytic lesions (holes in bone, seen with PET-CT). We need a technique for predicting lytic lesions via imaging.
- Denosumab retrospective study in pts w CRCL<30, give every mo vs every 3 mos?

Immune Therapy

- IMWG is building a database of immunotherapy results that will support future proposals such as Real-world experiences with BlenRep.
- Future – Immune Reconstitution

Mass Spectrometry

- Mass spec, a blood test, is more sensitive than IFE (Immunofixation) and "complementary" to NGS/NGF for MRD testing. Mass spec has about a 20-30% discordance with NGS/NGF. For MRD- via NGS/NGF but Mass Spec+, Dr Morrie Gertz is calling these patients VGPR.